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Articles

Giant Cyclophanes Built from Polyphenyl Aromatic Substructures

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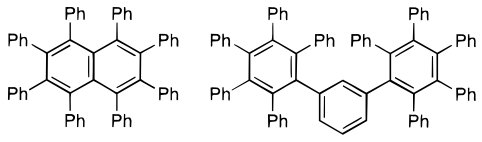
Two very large cyclophanes (**3**, $C_{132}H_{92}O_8S_4$; **4**, $C_{172}H_{120}O_8S_4$) were prepared by means of short syntheses (~5 steps) from commercial starting materials. In each of these cyclophanes, two octaphenylnaphthalene subunits or two 1,3-bis(pentaphenylphenyl)benzene subunits were tethered to form the final macrocycle. X-ray analysis of **3** shows it to have a collapsed conformation, but molecules of **4** have large central cavities which are aligned in the crystal to form wide, solvent-containing channels.

Polyphenyl aromatic compounds are excellent building blocks from which to construct robust nanostructures with well-defined conformations, often by means of short syntheses. A very recent review of such "polyphenylene nanostructures" shows a remarkable diversity of sizes and shapes.[1] In general, such polyphenyl aromatics are more densely substituted, and possibly have greater rigidity, than the majority of dendrimers,[2] catenanes,[3] or other deviously connected[4] molecules featuring aromatic substructures. Our own recent work with polyphenyl aromatic compounds has focused on the preparation and structural characterization of twisted polycyclic aromatic ribbons[5,6] and large molecular clefts.[7,8] In the latter case, where the principle substructures are derivatives of hexaphenylbenzene or octaphenylnaphthalene, the syntheses are very short and the overall yields can be quite good, and these features encouraged us to employ these polyphenyl aromatics for the construction of a new class of cyclophanes with large central cavities. In the present work we describe the synthesis and crystallographic characterization of two giant cyclophanes (**3** and **4**, Scheme 1) formed from easily prepared derivatives of octaphenylnaphthalene (**1**) and 1,3-bis(pentaphenylphenyl)benzene (**2**).



1 **2**

Results

Octaphenylnaphthalene-Based Cyclophanes. A cyclophane containing face-to-face octaphenylnaphtha-

(1) Berresheim, A. J.; Müller, M.; Müllen, K. *Chem. Rev.* **1999**, *99*, 1747−1785.
(2) (a) Bosman, A. W.; Janssen, H. M.; Meijer, E. W. *Chem. Rev.* **1999**, *99*, 1665−1688. (b) Newkome, G. R.; He, E.; Moorefield, C. N. *Chem. Rev.* **1999**, *99*, 1689−1746.
(3) Raymo, F. M.; Stoddart, J. F. *Chem. Rev.* **1999**, *99*, 1643−1663.
(4) Sritana-Anant, Y.; Seiders, T. J.; Siegel, J. S. *Top. Curr. Chem.* **1998**, *196*, 1−43.
(5) Qiao, X.; Padula, M. A.; Ho, D. M.; Vogelaar, N. J.; Schutt, C. E.; Pascal, R. A., Jr. *J. Am. Chem. Soc.* **1996**, *118*, 741−745.
(6) Qiao, X.; Ho, D. M.; Pascal, R. A., Jr. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1531−1532.
(7) Tong, L.; Ho, D. M.; Vogelaar, N. J.; Schutt, C. E.; Pascal, R. A., Jr. *Tetrahedron Lett.* **1997**, *38*, 7−10.
(8) Tong, L.; Ho, D. M.; Vogelaar, N. J.; Schutt, C. E.; Pascal, R. A., Jr. *J. Am. Chem. Soc.* **1997**, *119*, 7291−7302.

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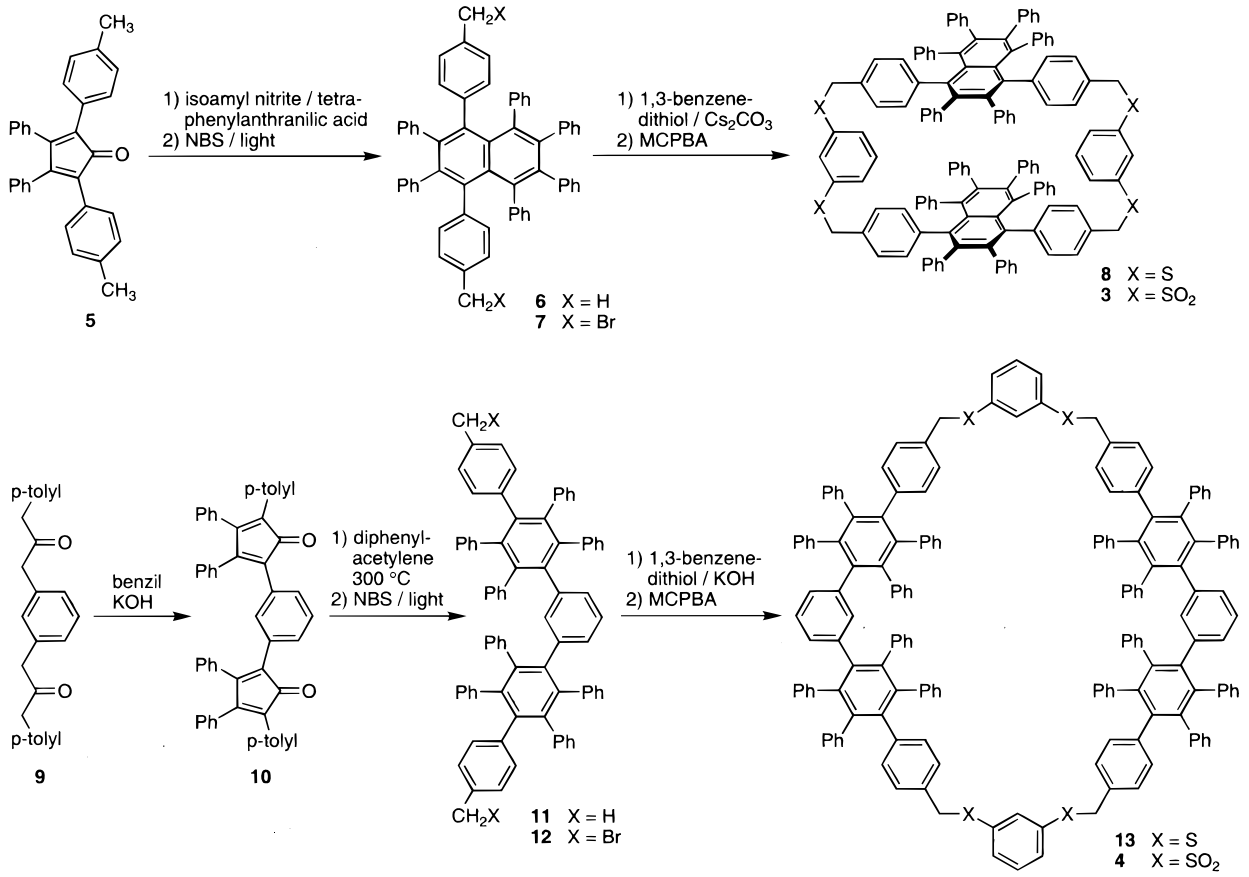
Scheme 1



lenes was our first target. Preliminary molecular mechanics calculations suggested that two seven-atom links between the *para* positions of the C(1) and C(4) phenyl groups in two molecules of **1** would permit those molecules to nestle comfortably so that the naphthalene faces and phenyl edges would define a central cavity. More importantly, such links would be too short to permit the two naphthalenes to swing away from each other. Methyl derivatives of **1** are easy to prepare,[9] so the dimethylated octaphenylnaphthalene **6** (Scheme 1) was chosen as the key substructure for preparation of this cyclophane. Compound **6** was prepared in one step from the known cyclopentadienone **5**[10] and 3,4,5,6-tetraphenylanthranilic acid[5] (via the aryne) in 83% yield, and NBS bromination gave the corresponding bis(bromomethyl) **7** in 73% yield. The synthesis of the cyclophane **8** was achieved easily, if in low yield (3.5%), by condensation of **7** with 1,3-benzenedithiol at high dilution in the presence of cesium carbonate. A trace of a trimeric cyclophane was also isolated, but it was characterized only by FAB MS. Finally, peracid oxidation of **8** gave the more highly crystalline tetrasulfone **3**.

But does the cyclophane contain a cavity? Molecular modeling can provide pleasing pictures of large macrocycles, and can serve as a useful guide to research, but compounds as large as **3** contain so many conformational degrees of freedom that X-ray structures are a virtual requirement for their reliable characterization. Cyclophane **3** crystallized easily from chloroform solution, but the crystals effloresced (decomposed by loss of solvent of crystallization) very rapidly upon removal from the mother liquor, and it was necessary to use a glass capillary mount for the X-ray data collection. The structure was solved without difficulty in the monoclinic space group *C*2/*c*, with $Z = 4$; that is, the cyclophane lies on a special position, in this case a crystallographic C_2 axis. The refinement was aided by the extra symmetry, but it was complicated by the presence of disordered chloroform molecules in the lattice (five $CHCl_3$ molecules per asymmetric unit). Indeed, the disordered solvent occupies 43% of the unit cell volume. Ultimately the SQUEEZE/BYPASS procedure[11] was employed to account for the solvent electron density, and subsequent refinement gave a satisfactory structure.

The molecular structure of cyclophane **3** is illustrated in Figure 1. The two naphthalene rings are slightly twisted (end-to-end twist 23.7°) and their mean planes are nearly parallel to one another (dihedral angle 7.0°). However, the naphthalenes are not directly on top of one another, but significantly slipped so that the edge-on phenyl substituents of one naphthalene partly fill the space above the opposite naphthalene, essentially eliminating any central cavity. The closest such contacts are between H(37) of the C(6) phenyl group and C(8A) and C(9A) of the opposite (symmetry-related) naphthalene (3.25 and 3.28 Å, respectively; the crystallographic numbering has been used). There is not sufficient space between the naphthalenes to accommodate even a single

(9) Qiao, X.; Pelczer, I.; Pascal, R. A., Jr. *Chirality* **1998**, *10*, 154−158.

(10) Mehr, L.; Becker, E. I.; Spoerri, P. E. *J. Am. Chem. Soc.* **1955**, *77*, 984−989.

(11) Van der Sluis, P.; Spek, A. L. *Acta Crystallogr., Sect. A* **1990**, *46*, 194−201.

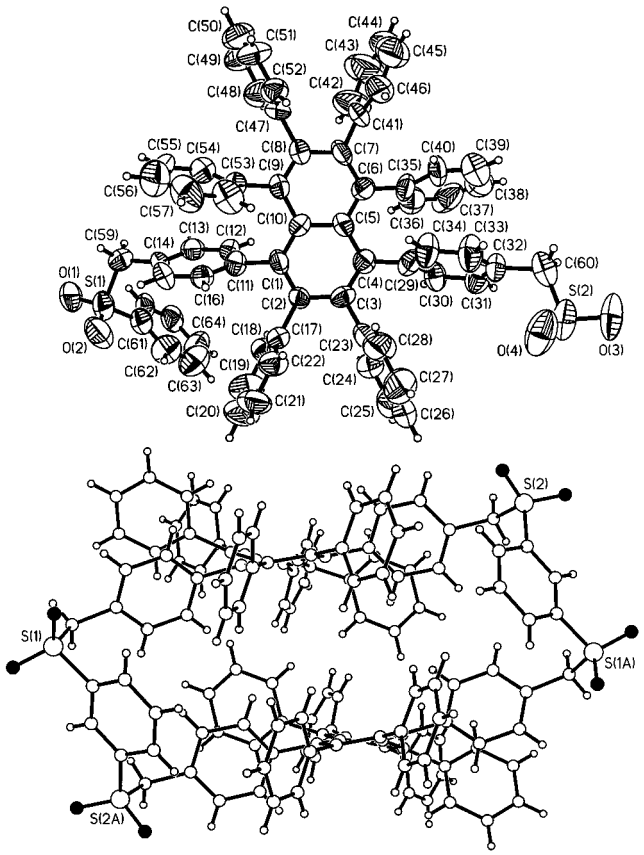


Figure 1. Molecular structure of cyclophane **3**. The crystallographically independent half-molecule is drawn with 50% probability thermal ellipsoids (top), and a ball-and-stick drawing of the full cyclophane is illustrated at the bottom.

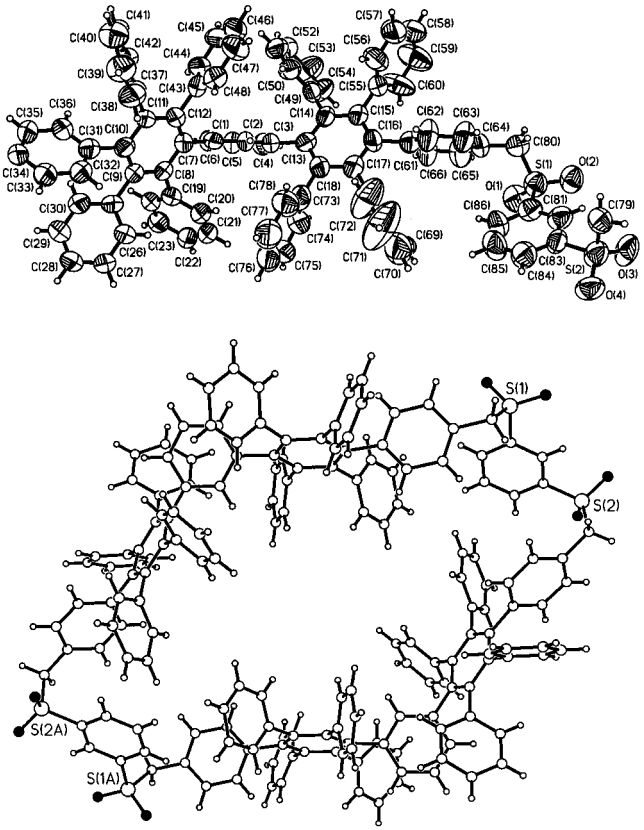


Figure 2. Molecular structure of cyclophane **4**. The crystallographically independent half-molecule is drawn with 50% probability thermal ellipsoids (top), and a ball-and-stick drawing of the full cyclophane is illustrated at the bottom.

molecule of solvent; all of the solvent included in the crystal lies outside the cyclophanes.

Bis(pentaphenylphenyl)benzene-Based Cyclophanes. The easy synthesis of **3** suggested that even larger cyclophanes might be prepared, but its X-ray structure emphasized the need to design a *noncollapsible* cavity. A good way to prepare such a cavity is to join two rigid molecular clefts. Large polyphenyl aromatics are ideal for this purpose, and 1,3-bis(pentaphenylphenyl)-benzene (**2**) seemed to be an especially good candidate. Two simple syntheses of **2** have been reported,[8,12] and its crystal structure shows it to possess a shallow cleft between the pentaphenylphenyl groups.[12] Molecular mechanics calculations indicated that a small spacer could be used to connect two molecules of **2** to form a relatively rigid, parallelogram-shaped molecule with a substantial central cavity. It was simplest to employ the same linking group that was used in the preparation of **3**, and thus a dimethyl derivative of **2** (compound **11**, Scheme 1) was chosen as our key substructure. The introduction of methyl groups at the desired positions in **2** was less efficient than with **1**, but the synthesis of **11** was still very simple. Diketone **9** was formed in a Claisen condensation of commercial starting materials in one step but in only 16% yield. Double aldol condensation with benzil gave the biscyclopentadienone **10** (42%), and a double Diels–Alder reaction with diphenylacetylene gave the desired hydrocarbon **11** (53%). NBS bromination of **11** was followed immediately by condensation with 1,3-benzenedithiol to give cyclophane **13** in 4.5% yield. Once again, this material was oxidized with MCPBA to give a more highly crystalline tetrasulfone (**4**).

Compound **4** deposited single crystals from DMSO–ether. These crystals, like those of **3**, contained substantial solvent of crystallization, but they only slowly effloresced upon removal from the mother liquor. As with **3**, compound **4** crystallized in the monoclinic space group *C*2/*c*, with $Z = 4$, but in this case the molecule lies on a crystallographic center of inversion. Both DMSO and ether molecules are present in the crystal, badly disordered, and occupying 36% of the unit cell volume. Once again, the SQUEEZE/BYPASS procedure was used to account for the solvent electron density to obtain a satisfactory refinement.

The molecular structure of cyclophane **4** is shown in Figure 2. The clefts of the two bis(pentaphenylphenyl)-benzene substructures face each other to form a large central cavity, with "corner-to-corner" distances across the interior, C(2)···C(2A) and C(85)···C(85A), of 12.5 and 17.5 Å, respectively. These distances are quite similar to those found in the MMFF-optimized[13,14] C_i-symmetric structure for compound **4**—13.5 and 17.2 Å, respectively—and and these two structures differ little in energy. For example, MMFF calculations indicate that compression of the C(2)···C(2A) distance from the "ideal" 13.5 Å to the crystallographically observed 12.5 Å requires only 0.8

(12) Müller, M.; Iyer, V. S.; Kübel, C.; Enkelmann, V.; Müllen, K. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1607–1610.

(13) Halgren, T. A. *J. Comput. Chem.* **1996**, *17*, 490–519.

(14) All molecular mechanics calculations were performed by using SPARTAN Version 5.0, Wavefunction, Inc., Irvine, CA.

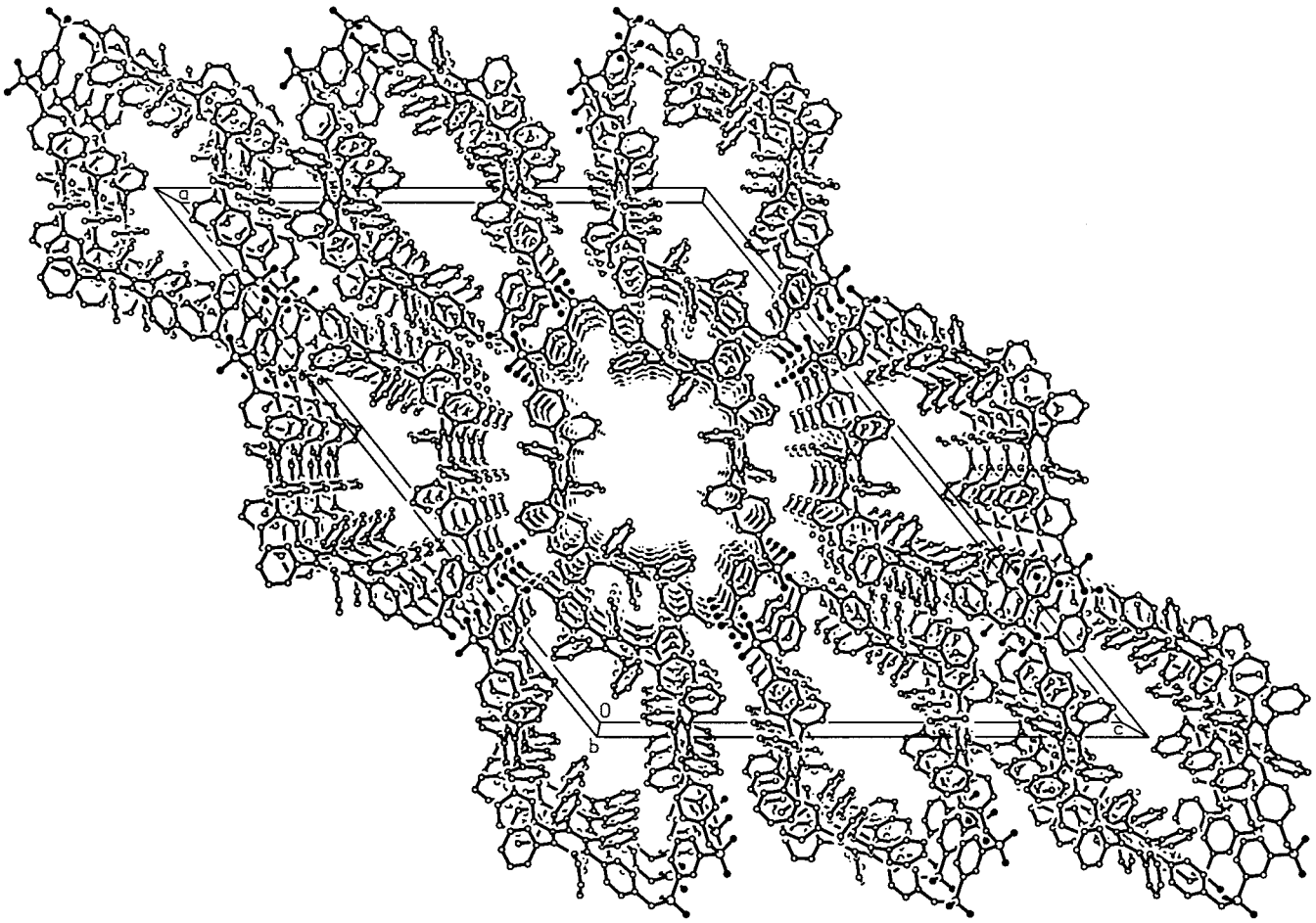


Figure 3. Unit cell and packing of cyclophane **4** viewed down the crystallographic *b* axis.

kcal/mol. However, to reduce substantially the size of the internal cavity by closing the C(2)···C(2A) distance to 10.0 Å requires 7.4 kcal/mol. It is for this reason that the cavity is effectively noncollapsible.

The symmetry-related hexaphenylbenzene subunits on opposite sides of the macrocycle are parallel to each other, and the mean planes of their central rings are 13.4 Å [C(7)−C(12) and C(7A)−C(12A)] and 9.2 Å [C(13)−C(18) and C(13A)−C(18A)] apart. These cavities are large enough to accommodate several solvent molecules, and in the crystal they are occupied by disordered ethers (not shown). Interestingly, the macrocycles pack to maximize contacts between hexaphenylbenzene subunits on adjacent molecules, with the result that the molecules stack with their cavities perfectly aligned to form infinite channels along the *b* axis of the crystals (Figure 3).

Discussion

As is usually the case with large polyphenyl polycyclic aromatic compounds, all of the large cyclophanes (**3**, **4**, **8**, and **13**), as well as their precursors, are quite soluble and easily handled. Although the overall synthetic yields of these molecules suffer in the macrocyclization steps, the synthesis of **8** (which contains 132 carbons) was achieved in only three steps from two known compounds (each of which was prepared in two steps from commercial starting materials), and the preparation of **13** (172 carbons) required only a five-step, linear synthesis. Oxidation of the thioethers (**8** and **13**) to the corresponding sulfones (**3** and **4**) was essentially quantitative.

Compounds **3** ($C_{132}H_{92}O_8S_4$) and **4** ($C_{172}H_{120}O_8S_4$) are among the largest crystallographically characterized cyclophanes. A search of the Cambridge Structural Database[15] found 23 different cyclophanes having more than 130 carbon atoms (transition metal complexes were excluded from the search). Twenty of these are carcerands from Cram's research group[16] or closely

(15) Allen, F. H.; Kennard, O.; Taylor, R. *Acc. Chem. Res.* **1983**, *16*, 146−153.

(16) The formulas of the cyclophanes described in each paper are given after the reference. (a) Tanner, M. E.; Knobler, C. B.; Cram, D. J. *J. Am. Chem. Soc.* **1990**, *112*, 1659−1660 [$C_{131}H_{112}O_{22}$]. (b) Sherman, J. C.; Knobler, C. B.; Cram, D. J. *J. Am. Chem. Soc.* **1991**, *113*, 2194−2204 [$C_{132}H_{112}O_{24}$]. (c) Helgeson, R. C.; Paek, K.; Knobler, C. B.; Maverick, E. F.; Cram, D. J. *J. Am. Chem. Soc.* **1996**, *118*, 5590−5604 [$C_{140}H_{128}O_{24}$]. (d) Helgeson, R. C.; Knobler, C. B.; Cram, D. J. *J. Am. Chem. Soc.* **1997**, *119*, 3229−3244 [$C_{140}H_{160}O_{24}$, $C_{144}H_{168}O_{24}$, $C_{148}H_{176}O_{24}$]. (e) Eid, C. N., Jr.; Knobler, C. B.; Gronbeck, D. A.; Cram, D. J. *J. Am. Chem. Soc.* **1994**, *116*, 8506−8515 [$C_{144}H_{120}O_{24}$, $C_{144}H_{128}O_{24}$]. (f) Robbins, T. A.; Knobler, C. B.; Bellew, D. R.; Cram, D. J. *J. Am. Chem. Soc.* **1994**, *116*, 111−122 [$C_{144}H_{136}O_{24}$]. (g) Byun, Y.-S.; Vadhat, O.; Blanda, M. T.; Knobler, C. B.; Cram, D. J. *Chem. Commun.* **1995**, 1825−1827 [$C_{144}H_{136}O_{28}$]. (h) Yoon, J.; Sheu, C.; Houk, K. N.; Knobler, C. B.; Cram, D. J. *J. Org. Chem.* **1996**, *61*, 9323−9339 [$C_{145}H_{138}O_{24}$, $C_{148}H_{136}O_{24}$]. (i) Yoon, J.; Knobler, C. B.; Maverick, E. F.; Cram, D. J. *Chem. Commun.* **1997**, 1303−1304 [$C_{148}H_{136}O_{24}$]. (j) Byun, Y.-S.; Robbins, T. A.; Knobler, C. B.; Cram, D. J. *Chem. Commun.* **1995**, 1947−1948 [$C_{148}H_{144}O_{24}$]. (k) Park, B. S.; Knobler, C. B.; Eid, C. N., Jr.; Warmuth, R.; Cram, D. J. *Chem. Commun.* **1998**, 55−56 [$C_{156}H_{152}O_{32}$]. (l) Cram, D. J.; Blanda, M. T.; Paek, K.; Knobler, C. B. *J. Am. Chem. Soc.* **1992**, *114*, 7765−7773 [$C_{160}H_{136}O_{24}$]. (m) Choi, H.-J.; Buhring, D.; Quan, M. L. C.; Knobler, C. B.; Cram, D. J. *Chem. Commun.* **1992**, 1733−1735 [$C_{160}H_{128}N_8O_{24}$]. (n) Quan, M. L. C.; Knobler, C. B.; Cram, D. J. *Chem. Commun.* **1991**, 660−662 [$C_{160}H_{120}O_{32}$]. (o) Von dem Bussche-Hunnefeld, C.; Buhring, D.; Knobler, C. B.; Cram, D. J. *Chem. Commun.* **1995**, 1085−1087 [$C_{208}H_{168}O_{24}$].

related compounds,[17] two are large hydrocarbons based on fluorene subunits,[18] and one is a tetrameric tetrapyrrole.[19] Compound **4** is larger than all but three of these compounds,[16m−o] and the use of polyphenyl aromatics as key substructures is unique to **3** and **4**.

Our intent was to design molecules with large cavities. Compound **3** retained sufficient conformational freedom to permit the cavity to collapse, but in **4** the relatively rigid, cleft-containing substructures force the macrocycle to remain open. Moreover, the central cavity in **4** is large enough to hold two or three small molecules side by side. It was also our hope that such cyclophanes would stack in the solid state so that their central cavities would form continuous channels through the crystal. It is extremely difficult to design the packing of molecular crystals, but in the case of **4**, this goal was met, whether by design or chance. The four slab-like, hydrophobic, polyphenyl aromatic sides of **4** favor the packing of these sides against each other, and as a consequence, the macrocycles' cavities are perfectly aligned to form channels in the crystal. These channels are wide enough that small molecules could pass each other within them, and thus the channel contents might be exchanged in the crystal if the crystals were sufficiently stable. If such a structure were *very* robust, then one would have the equivalent of a zeolite with a completely hydrophobic interior.

Unfortunately, crystals of **4** do decompose upon loss of solvent. We suspect that it is the loss of solvent *outside* the channels that compromises the structural integrity, not the loss of ether in the "noncollapsible" channels. We have previously reported one example of an extremely stable, channel-containing crystal of a polyphenyl polycyclic aromatic compound—decaphenylanthracene[5]—where the crystals melt above 400 °C, and for which NMR and X-ray studies show the channels to be incompletely filled with solvent. Unfortunately, the channels in decaphenylanthracene are too narrow to permit solvent exchange. Perhaps in the future it will be possible to modify the exterior surface of **4** so that it packs in the crystal without any interstitial solvent molecules to form an extremely stable structure with large zeolite-like channels.

Experimental Section

1,4-Di(*p*-tolyl)-2,3,5,6,7,8-hexaphenylnaphthalene (6). A solution of 2,5-di(*p*-tolyl)-3,4-diphenylcyclopentadienone[10] (**5**; 1.22 g, 2.96 mmol) in 1,2-dichloroethane (40 mL) was heated to reflux under argon. A solution of isoamyl nitrite (1.5 mL) in dichloroethane (80 mL) was added, followed by the dropwise addition of a solution of tetraphenylanthranilic acid[5] (1.73 g, 4.10 mmol) in dichloroethane (140 mL) over 1.5 h. After the resulting solution was heated for 1 h more, the reaction was terminated by addition of ethanol (55 mL) and 1% aqueous KOH (160 mL). $CHCl_3$ was added; then the organic layer was separated, washed with aqueous $NaHCO_3$, dried over $MgSO_4$, and concentrated to dryness. The residue was recrystallized twice from benzene−ethanol to yield **6** as off-white crystals (1.88 g, 2.46 mmol, 83%): mp 289−291 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 2.01 (s, 6 H), 6.37 and 6.42 (AA′BB′ system, 8 H), 6.64 (m, 30 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.9, 124.2, 124.7, 125.8, 126.0, 126.1, 126.8, 128.3, 131.2, 131.86, 131.93, 133.5, 133.7, 138.2, 138.3, 139.0, 139.66, 139.74, 140.7, 140.8, 142.2 (21 of 22 expected resonances observed); MS *m*/*z* 764 (M^+, 100), 687 (M − C_6H_5, 33), 673 (M − $CH_3C_6H_4$, 14); exact mass 764.3428, calcd for $C_{60}H_{44}$ 764.3443.

1,4-Bis[*p*-(bromomethyl)phenyl]-2,3,5,6,7,8-hexaphenylnaphthalene (7). Compound **6** (1.44 g, 1.88 mmol), NBS (0.67 g, 3.8 mmol), and a few bits of AIBN were heated to reflux in CCl_4 (30 mL) under a tungsten lamp for 8 h. The hot reaction mixture was filtered and rinsed with CCl_4. CH_2Cl_2 was added, and the solution was washed with saturated $NaHCO_3$, dried over Na_2SO_4, and concentrated to dryness. The residue was chromatographed on silica gel (1:1 $CHCl_3$−hexanes). The appropriate fractions were combined and concentrated, and the resulting solid was recrystallized twice from CH_2Cl_2−methanol to yield **7** as colorless needles (1.26 g, 1.37 mmol, 73%): mp 272−274 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 4.22 (s, 4 H), 6.51−6.75 (m, 38 H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 34.3, 124.9, 126.1, 126.2, 126.3, 126.4, 126.9, 131.0, 131.9, 132.1, 133.1, 133.3, 137.7, 138.2, 139.6, 139.9, 140.2, 140.3, 141.7, 142.3 (20 of 22 expected resonances observed); FAB MS *m*/*z* 923 (M[^{79}Br^{81}Br] + H, 100), 844 (M + H − Br, 44).

Cyclophane 8. Two solutions were prepared: (1) compound **7** (0.55 g, 0.60 mmol) and 1,3-benzenedithiol (0.085 g, 0.60 mmol) were dissolved in 150 mL of benzene, and (2) Cs_2CO_3 (0.78 g, 2.4 mmol) was dissolved in ethanol (100 mL). Solutions 1 and 2 were separately and simultaneously added to a refluxing solution of benzene (150 mL) and ethanol (50 mL) over 2 h under argon. After being heated for 1.5 days, the mixture was cooled and the solvent was removed under reduced pressure. $CHCl_3$ (500 mL) was added, and the resulting mixture was heated at reflux for 2.5 h and then filtered while hot. After concentration, the residue was chromatographed on silica gel (2:1 $CHCl_3$−hexanes). The fractions containing the desired cyclophane **8** were combined and concentrated. Further purification of this material by preparative TLC (silica gel GF; solvent 2:1 $CHCl_3$−cyclohexane) gave **8** as a colorless solid (19 mg, 11 μmol, 3.5%): mp 230 °C dec; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.69 (s, 8 H), 6.26 and 6.38 (AA′BB′ system, 16 H), 6.46 (t, J = 8 Hz, 8 H), 6.51 (m, 16 H), 6.56 (m, 14 H), 6.61 (dd, J = 8 Hz, 2 Hz, 4 H), 6.70 (m, 20 H), 6.81 (td, J = 8 Hz, 2 Hz, 4 H), 7.42 (t, J = 2 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 39.6, 124.5, 124.76, 124.80, 126.0, 126.1, 126.4, 126.7, 128.4, 131.0, 131.1, 131.6, 131.9, 132.0, 133.0, 134.0, 135.3, 135.6, 138.1, 138.4, 140.1, 140.39, 140.45, 140.49, 140.9, 141.9 (26 of 26 expected resonances observed); FAB MS *m*/*z* 1806 (M[$^{13}C_1$] + H, 100), 1665 (M − $C_6H_4S_2$, 41). A trace of a trimeric cyclophane was also isolated, but it was characterized only by its FAB MS: *m*/*z* 2710 (M[$^{13}C_3$] + H, 30), 764 (100).

Cyclophane 3. A solution of cyclophane **8** (7.2 mg, 4.0 μmol) in CH_2Cl_2 (0.5 mL) was placed in an ice bath. Freshly purified MCPBA (5.4 mg) in CH_2Cl_2 (0.5 mL) was added dropwise. After the ice bath was removed, the flask was placed under an argon atmosphere and stirred at room temperature for 48 h. Some crystalline material was deposited during this time. $CHCl_3$ (20 mL) was added, dissolving everything. The solution was washed with dilute $Na_2S_2O_3$ and saturated Na_2CO_3, and it was dried

(17) Ungaro, R.; Pochini, A.; Andreetti, G. D.; Ugozzoli, F. *J. Inclusion Phenom.* **1985**, *3*, 409−420 [$C_{144}H_{224}O_{16}$].

(18) Ipaktschi, J.; Hosseinzadeh, R.; Schlaf, P.; Dreiseidler, E.; Goddard, R. *Helv. Chim. Acta* **1998**, *81*, 1821−1834 [$C_{144}H_{112}$, $C_{160}H_{144}$].

(19) Khoury, R. G.; Jaquinod, L.; Nurco, D. J.; Pandey, R. K.; Senge, M. O.; Smith, K. M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2496−2499 [$C_{140}H_{136}O_{28}$].

over $MgSO_4$. Concentration yielded cyclophane **3** as a colorless solid (8 mg) which exhibited a single component upon TLC analysis ($CHCl_3$, R_f 0.05). Crystals of the tetrasulfone **3** suitable for X-ray analysis were obtained from $CHCl_3$: mp > 350 °C (darkens gradually above 200 °C); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.95 (d, J = 15 Hz, 4 H), 4.16 (d, J = 15 Hz, 4 H), 5.33 (d, J = 7 Hz, 4 H), 6.14−7.00 (m, 78 H), 8.38 (s, 2 H); FAB MS m/z 1934 (M[$^{13}C_1$] + H, 80), 1729 (M − $C_6H_4S_2O_4$, 31), 460 (100).

1,3-Bis[3-(*p*-tolyl)-2-oxopropyl]benzene (9). Ether (50 mL) and *n*-butyllithium (2.5 M in hexanes, 8.8 mL, 22.0 mmol) were stirred under argon in a two-necked flask cooled in an ice bath. Diisopropylamine (2.1 mL, 15 mmol) was added, and after the resulting solution was stirred for 30 min, methyl (*p*-tolyl)acetate (3.1 g, 18.9 mmol) was added dropwise. The resulting solution was stirred for 15 min. Dimethyl 1,3-benzenediacetate (2.0 g, 9.0 mmol) was then added dropwise, the ice bath was removed, and the mixture was stirred overnight at room temperature. The reaction mixture was poured into 1 N HCl, and the layers were separated. The aqueous layer was extracted twice with ether, and the combined ether extracts were washed with water and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was heated with 6 N HCl (20 mL) and acetic acid (150 mL) for 7 h. After cooling and removal of the solvent, the residue was extracted with ether. The extract was washed with aqueous $NaHCO_3$ and dried over Na_2SO_4. After concentration, the residue was chromatographed on silica gel (4:1 hexanes−ethyl acetate). The fractions containing the desired product (R_f 0.51) were combined and concentrated to afford white solid **9** (530 mg, 1.43 mmol, 16%): mp 77−78 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 2.32 (s, 6 H), 3.66 (s, 4 H), 3.67 (s, 4 H), 6.90 (br s, 1 H), 7.03 and 7.11 (AA′BB′ system, 8 H), 7.02 (m, 2 H), 7.25 (t, J = 8 Hz, 1 H); MS m/z 370 (M^+, 19), 105 (M − C_8H_9, 100); exact mass 370.1912, calcd for $C_{26}H_{26}O_2$ 370.1933.

1,3-Bis[2-oxo-3-(*p*-tolyl)-4,5-diphenylcyclopenta-1,4-dienyl]benzene (10). Compound **9** (400 mg, 1.1 mmol) and benzil (454.4 mg, 2.16 mmol) were dissolved in ethanol (12 mL). In a separate test tube, KOH (256 mg, 4.56 mmol) was dissolved in water (0.25 mL), and ethanol (2 mL) was added. Half of this KOH solution was added dropwise to the solution of diketone **9** and benzil at room temperature. The reaction flask was then immersed in a water bath at 85 °C, and the other portion of the KOH solution was added dropwise. The resulting solution was heated with gentle swirling for 15 min. A purple precipitate formed, and after it was cooled to room temperature and subsequent refrigeration, the product was collected by suction filtration and washed with cold ethanol. TLC analysis (4:1 hexanes−ethyl acetate) showed one major spot at R_f 0.66. Recrystallization of this material from ethanol afforded deep purple crystals of **10** (323 mg, 0.450 mmol, 42%): mp 290−292 °C; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 2.38 (s, 6 H), 7.13 (m, 32 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 22.0, 125.8, 125.9, 128.3, 128.5, 128.6, 128.9, 129.1, 129.5, 129.9, 130.0, 130.7, 131.5, 132.7, 133.7, 134.1, 138.0, 154.2, 155.4, 201.0 (20 of 22 expected peaks observed); MS m/z 718 (M^+, 100), 690 (M − CO, 10); exact mass 718.2890, calcd for $C_{54}H_{38}O_2$ 718.2872.

1,3-Bis[4-(*p*-tolyl)-2,3,5,6-tetraphenylphenyl]benzene (11). Compound **10** (200 mg, 0.28 mmol) and diphenylacetylene (200 mg, 1.1 mmol) were heated in a screw-capped Pyrex tube for 3.5 h at 300 °C. The tube was cooled to room temperature, and acetone (∼1.5 mL) was added to precipitate the product. The off-white precipitate was collected by suction filtration. TLC analysis (9:1 hexanes−ethyl acetate) showed one major component (R_f 0.64). The product **11** was dried under vacuum overnight (151 mg, 0.148 mmol, 53%): mp > 350 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.06 (s, 6 H), 6.20 (m, 6 H), 6.75 (m, 46 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.2, 125.0, 125.2, 126.5, 127.1, 127.4, 129.1, 131.3, 131.5, 131.6, 131.7, 134.5, 136.1, 137.8, 139.0, 139.1, 140.1, 140.4, 140.8, 141.0, 141.2 (21 of 21 expected peaks observed); FAB MS m/z 1019 (M + H, 100).

Table 1. Crystallographic Data for Compounds 3 and 4

	3	**4**
chemical formula	$C_{132}H_{92}O_8S_4$·10$CHCl_3$	$C_{172}H_{120}O_8S_4$·2C_2H_6OS·7$C_4H_{10}O$
fw	3127.98	3118.02
cryst size (mm)	0.42 × 0.38 × 0.12	0.38 × 0.12 × 0.10
space group	*C*2/*c* (no. 15)	*C*2/*c* (no. 15)
a, Å	28.7412(8)	49.754(7)
b, Å	15.4254(5)	11.6954(11)
c, Å	38.3795(11)	39.053(6)
α, deg	90	90
β, deg	111.3650(10)	129.320(3)
γ, deg	90	90
V, Å^3	15846.0(8)	17580(4)
Z	4	4
ρ_{calcd}, g/cm^3	1.311	1.178
μ, mm^{-1}	0.62	0.14
T, K	298(2)	170(2)
θ_{max}, deg	28.3	22.5
no. of reflections		
total	36730	85211
unique	17119	11364
obsd [$I > 2\sigma(I)$]	4785	4484
$R(F)$ (obsd data)[a]	0.0791	0.0595
$Rw(F^2)$ (obsd data)[a]	0.1643	0.1342
S (obs. data)[a]	1.265	1.203
$R(F)$ (all data)[a]	0.2296	0.1572
$wR(F^2)$ (all data)[a]	0.2092	0.1611
S (all data)[a]	0.823	0.858

[a] $R(F) = \sum||F_o| - |F_c||/\sum|F_o|$; $R_w(F^2) = [\sum w(F_o^2 - F_c^2)^2/\sum w(F_o^2)^2]^{1/2}$; S = goodness-of-fit on $F^2 = [\sum w(F_o^2 - F_c^2)^2/(n - p)]^{1/2}$, where n is the number of reflections and p is the number of parameters refined.

Cyclophane 13. Compound **11** (250 mg, 0.25 mmol) and NBS (44.5 mg, 0.25 mmol) were heated to reflux in CCl_4 (35 mL), and heating was continued under a tungsten lamp for 4 h. The resulting brown mixture was cooled to room temperature and filtered. After concentration of the filtrate on a rotary evaporator, the residue was chromatographed on silica gel (9:1 hexanes−ethyl acetate) to yield a roughly 2:1 mixture of the desired dibromide **12** and starting material **11** (202 mg total) as judged by ^{1}H NMR analysis. This material was used without further purification. Two solutions were then prepared: (1) 1,3-benzenedithiol (24.2 mg, 0.170 mmol) and crude compound **12** (200 mg, nominally 0.17 mmol) were dissolved in benzene (30 mL), and (2) KOH (28.7 mg, 0.435 mmol) was dissolved in ethanol (30 mL). Solutions 1 and 2 were then separately and simultaneously added dropwise over 2 h to a refluxing mixture of ethanol (80 mL) and benzene (20 mL) under argon. The resulting mixture was heated at reflux overnight. After cooling, the solvent was removed under reduced pressure, and the residue was fractionated by preparative TLC (silica gel GF; solvent 2:1 CH_2Cl_2−hexanes). The

material with R_f 0.25 was collected and shown by MS and ^{1}H NMR analysis to be crude cyclophane **13**. A second purification by preparative TLC yielded **13** as a white solid (13 mg, 5.6 μmol, 4.5% from **11**): ^{1}H NMR ($CDCl_3$, 270 MHz) δ 3.65 (s, 8 H), 6.80 (m, 112 H); FAB MS *m*/*z* 2315 (M[$^{13}C_2$] + H, 48), 2175 (M − $C_6H_4S_2$, 22), 1048 ($C_{80}H_{56}S^+$, 100).

Cyclophane 4. A solution of cyclophane **13** (7.0 mg, 3.0 μmol) in CH_2Cl_2 (0.5 mL) was placed in an ice bath. Freshly purified MCPBA (4.0 mg) in CH_2Cl_2 (0.5 mL) was added dropwise. After the ice bath was removed, the flask was placed under an argon atmosphere and stirred at room temperature for 48 h. $CHCl_3$ was added to the mixture, and it was washed with saturated Na_2CO_3 and dried over $MgSO_4$. After removal of the solvent, a white solid was obtained (10 mg). Crystals of the tetrasulfone **4** suitable for X-ray analysis were grown from a DMSO−ether solution of the crude solid: mp > 350 °C (darkens slowly above 200 °C); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.00 (s, 8 H), 6.09−6.27 (m, 20 H), 6.62−7.00 (m, 142 H), 8.30 (s, 2 H); FAB MS *m*/*z* 2443 (M[$^{13}C_2$] + H, 50), 1017 ($C_{80}H_{57}^+$, 35), 363 (100).

General X-ray Crystallographic Procedures. X-ray data were collected by using graphite-monochromated Mo Kα radiation (0.710 73 Å) on either a Siemens SMART CCD diffractometer (compound **3**) or a Nonius KappaCCD diffractometer (**4**). The diffraction data were processed by using Siemens SAINT for the former structure, and by using DENZO[20] for the latter. Both were solved by using Siemens SHELXTL,[21] and both were refined by full-matrix least-squares on F^2 using SHELXTL or SHELXTL-93.[22] All non-hydrogenatoms were refined anisotropically, and hydrogens were included with a riding model. Due to the very large number of disordered solvent molecules present in each crystal, the SQUEEZE/BYPASS procedure[11] implemented in PLATON-96[23] was employed to account for disordered solvent electron density. Specific crystal, reflection, and refinement data are contained in Table 1, and full details are provided in the Supporting Information.

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Supporting Information Available: Crystal structure reports for **3** and **4** (including full experimental details, tables, and figures), and ^{1}H NMR spectra and selected ^{13}C NMR spectra of compounds **3**, **4**, **6**−**11**, and **13**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(20) Otwinowski, Z.; Minor, W. *Methods Enzymol.* **1997**, *276*, 307−326.

(21) Sheldrick, G. M. SHELXTL Version 5, Siemens Analytical X-ray Instruments, Madison, Wisconsin, 1996.

(22) Sheldrick, G. M. SHELXL-93. Program for the Refinement of Crystal Structures. University of Gottingen, Germany, 1993.

(23) Spek, A. L. *Acta Crystallogr., Sect. A* **1990**, *46*, C34.